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Letter to the Editor

Why would procalcitonin perform better in patients with a SOFA-score less than 8?

We read with great interest the meta-analysis by Peng and colleagues published in the *International Journal of Infectious Diseases*, in which they questioned the effectiveness of procalcitonin (PCT)-guided antibiotic therapy (Peng et al., 2019). They combined 16 randomized controlled trials (RCT), including 6452 critically ill patients with infections, and concluded that PCT-guided antibiotic therapy does not lead to a decreased short-term mortality. They also concluded that PCT-guided cessation of antibiotics only reduces short-term mortality in patients with a Sequential Organ Failure Assessment (SOFA) score of <8. It was, therefore, suggested that PCT-guided antibiotic therapy would be better suited to patients without multiple organ failure in the emergency department or general ward. Unfortunately, we think that this conclusion is neither correctly derived from the available data nor plausible!

The question regarding whether the severity of illness, as measured by the SOFA score, influences the effect of antibiotic treatment in all RCTs on PCT-guided therapy, is a valid research question. However, analyses should have been done at the individual patient level. Indeed, a recent patient-level meta-analysis on PCT-guided antibiotic therapy in 4482 septic patients in the intensive care unit (ICU), by Wirz and colleagues, showed that 30-day mortality was lower in the PCT-guided group (Wirz et al., 2018). Furthermore, when patients were divided into three subgroups by organ failure (SOFA 0 to 6, 7 to 10, and 10 to 24), the effects on mortality persisted. In our SAPS-trial on PCT guidance (De Jong et al., 2016), we included 1546 ICU patients and we demonstrated a significant reduction in 28-day mortality in the PCT group ($p = 0.007$). This effect on mortality persisted in the 587 patients with a SOFA score of ≥ 8 ($p = 0.024$).

Moreover, why should PCT-guided antibiotic therapy be better suited to patients in the emergency department and general ward or only patients with a SOFA score of <8? Obviously there are numerous non-infectious inflammatory processes, e.g. trauma or surgery, in which PCT can be elevated. Such conditions are frequently seen in emergency departments and general wards, but can also be encountered in the ICU. These conditions were well balanced between the two groups in previous meta-analyses. We therefore conclude that antibiotics should be started when an infection is suspected and that PCT is particularly suited for the cessation of antibiotic treatment, and we want to warn care-givers that the sensitivity and specificity of a single PCT measurement in

the emergency department, general ward, or ICU are not high enough to start or withhold antibiotics based on PCT alone.

Author contributions

All authors (JvO, MN, EdJ, BB, and DL) made equal contributions.

Ethics approval and consent to participate

Not applicable.

Consent for publication

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Availability of data and material

Not applicable.

Competing interests

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